

Appendix E

Magnesium Sulfate IV for Refractory Migraine in the ED

Specific Care Question :

In the pediatric patient diagnosed with a refractory migraine, what is the efficacy of intravenous magnesium sulfate to decrease migraine pain in the Emergency Department?

Question Originator:

Migraine Therapy in the ED CPG Team

Plain Language Summary from The Office of Evidence Based Practice:

Based on very low quality evidence, the Migraine in the ED CPG team makes a conditional recommendation against treating with IV magnesium sulfate as a first line treatment for refractory migraine in the ED. The desirable effect of reducing symptom scores were not apparent and the proportion of subjects who incurred an adverse event was greater. The evidence to support this recommendation is graded as very low quality (see Table 1). The recommendation is based on the systematic review with meta-analysis by Choi & Parmar (2014) that includes five RCTs. The evidence is graded as very low quality due to indirectness (adult populations), inconsistency (the dose of IV magnesium varied across studies), and imprecise findings (the number of subjects studied in individual studies is low).

Literature Synthesis

Choi & Parmar (2014) performed a systematic review. The meta-analysis showed for the outcome "Difference in Pain within 60 Minutes" there was no difference between the groups treated with magnesium sulfate (IV) and placebo or metoclopramide, $RR = 1.05$ 95% CI [0.70, 1.57]. When a sensitivity analysis was done to see if there was a difference if the control group received metoclopramide or normal saline, the estimate of the effect still showed no difference between the groups. (See Figure 1)

For the outcome "Need for Rescue Medication" there was no difference between the groups treated with magnesium sulfate (IV) and placebo or metoclopramide, $RR = 0.98$ 95% CI [0.80, 1.22]. Again, when sensitivity analysis was done to see if normal saline or metoclopramide were used as control, there was no difference in the estimate of the effect. (See Figure 2)

For the outcome "Adverse Events" there were significantly more adverse events, predominantly flushing, followed by dizziness and burning at the IV site for those treated with magnesium sulfate $RR = 2.53$ 95% CI [1.53, 4.18]. When a sensitivity analysis was done to see if normal saline or metoclopramide was used as control, there were still significantly more adverse events in the groups treated with magnesium sulfate (IV). (See Figure 3)

Dose: Magnesium sulfate (IV) -50mg/kg (max 2gm) IV over one hour

EBP team member responsible for reviewing, synthesizing, and developing this literature:

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Search Strategy and Results:

Searches performed on March 10 2014

PubMed

"Migraine Disorders/drug therapy"[Mesh] AND (("Cohort Studies"[Mesh] OR (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR Controlled Clinical Trial[ptyp] OR Guideline[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb])) AND ("2009/01/01"[PDAT] : "2014/12/31"[PDAT]) AND "humans"[MeSH Terms] AND English[lang] AND ("infant"[MeSH Terms] OR "child"[MeSH Terms] OR "adolescent"[MeSH Terms]))

EMBASE

'**migraine**'/exp/mj/dm_dt AND ([internal medicine]/lim OR [neurology and psychiatry]/lim OR [pediatrics]/lim OR [pharmacology and pharmacy]/lim) AND ([infant]/lim OR [preschool]/lim OR [school]/lim OR [child]/lim OR [adolescent]/lim) AND [humans]/lim AND [english]/lim AND [abstracts]/lim AND [embase]/lim AND [2009-2014]/py

Studies included in this review:

Choi & Parmar (2014)

Study excluded in this review and reason for exclusion

Study	Reason for exclusion
Gertsch et al., 2014	Although the it is a pediatric case series of children treated with magnesium sulfate (IV) for migraine, subjects were treated with other medications such as ketorolac, diphenhydramine and prochlorperazine, or ondansetron prior to magnesium IV

Method Used for Appraisal and Synthesis:

The Cochrane Collaborative computer program, Review Manager (RevMan 5.3.5) (Higgins & Green, 2011), was used to recreate the meta-analysis reported in Choi (2014). GradePro ws used to assess the methodological quality of the meta-analysis.

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Characteristics of included study:

Tables:

Table 1. Grade Summary of Included Studies Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate IV	Other treatments	Relative (95% CI)	Absolute	
Headache response assessed less than or equal to 60 minutes											
5	randomized trials	no serious risk of bias	serious ^{1,2}	no serious indirectness	very serious ³	none	87/123 (70.7%)	84/131 (64.1%)	OR 0.95 (0.22 to 4.16)	12 fewer per 1000 (from 359 fewer to 240 more)	VERY LOW
Adverse effects											
4	randomized trials	no serious risk of bias	serious ¹	no serious indirectness	very serious ³	none	35/94 (37.2%)	14/101 (13.9%)	OR 4.93 (2.22 to 10.94)	304 more per 1000 (from 125 more to 499 more)	VERY LOW
Need for rescue medications											
3	randomized trials	no serious risk of bias	serious ¹	no serious indirectness	very serious ³	none	50/78 (64.1%)	46/79 (58.2%)	OR 1.32 (0.66 to 2.66)	66 more per 1000 (from 103 fewer to 205 more)	VERY LOW

¹ Various medications were used as comparison.

² The I2 statistic is 80%, less than 50% is desired

³ Low number of events, with low numbers of subjects in each group

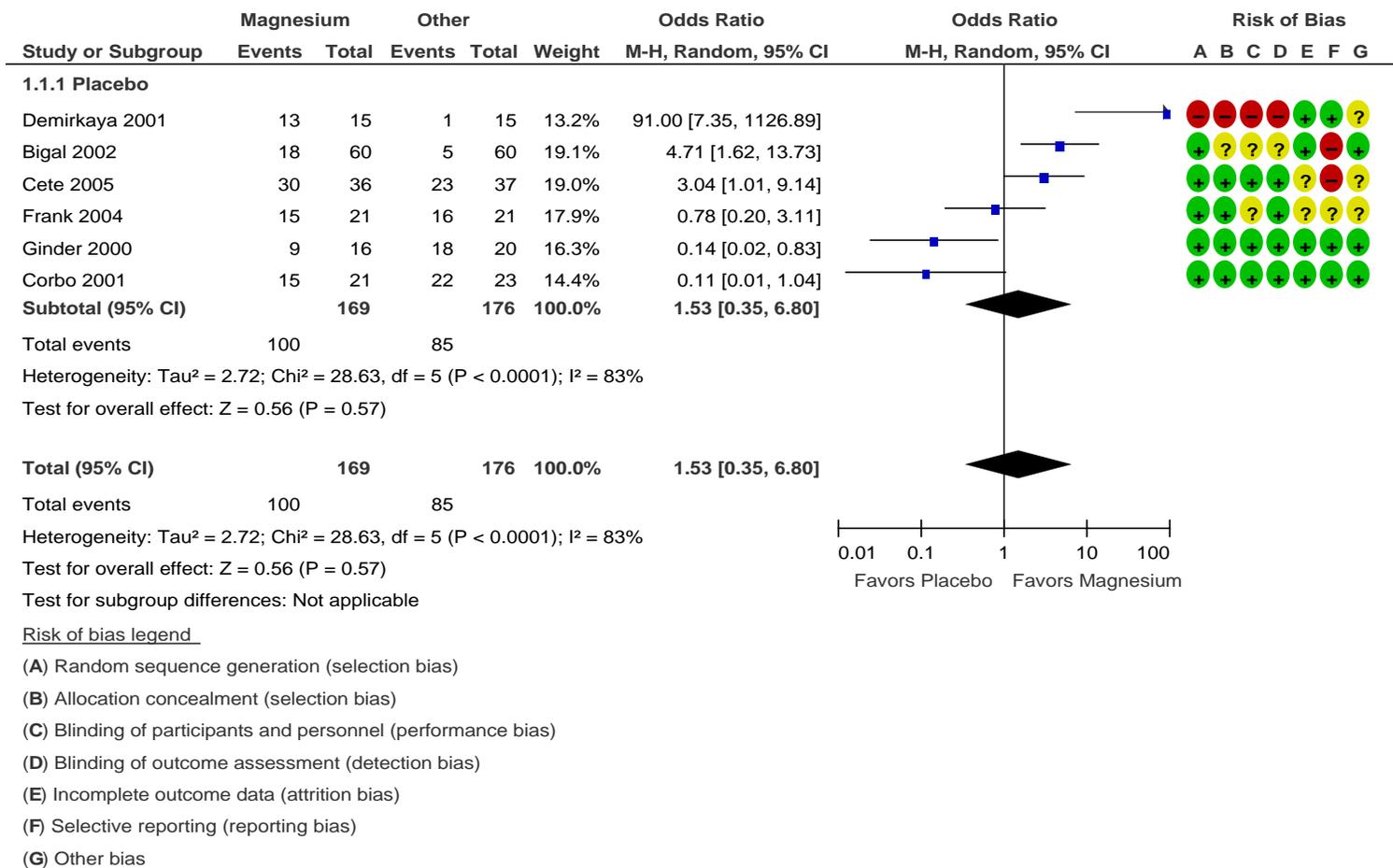
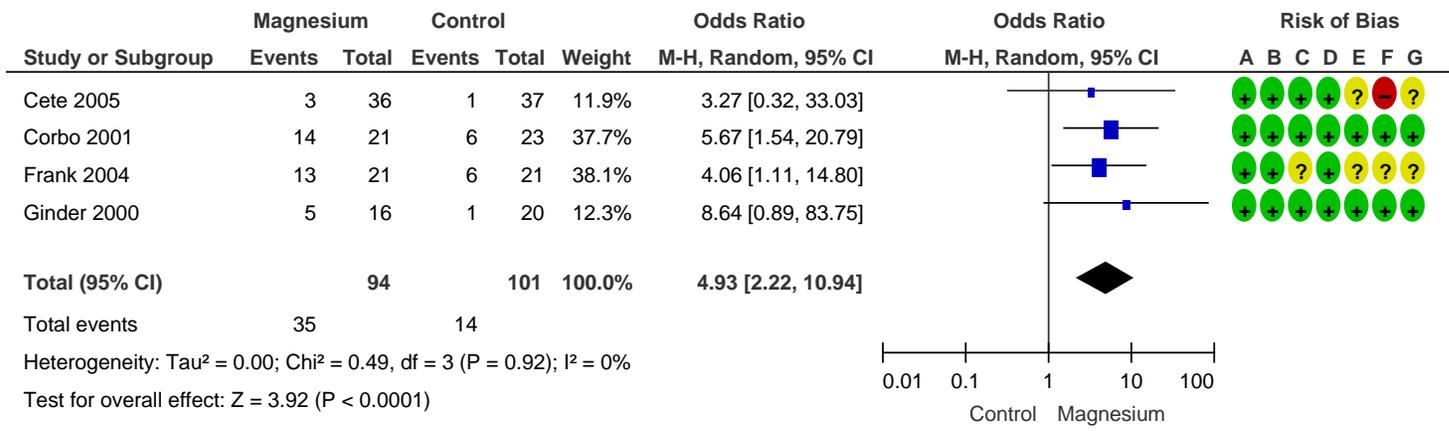


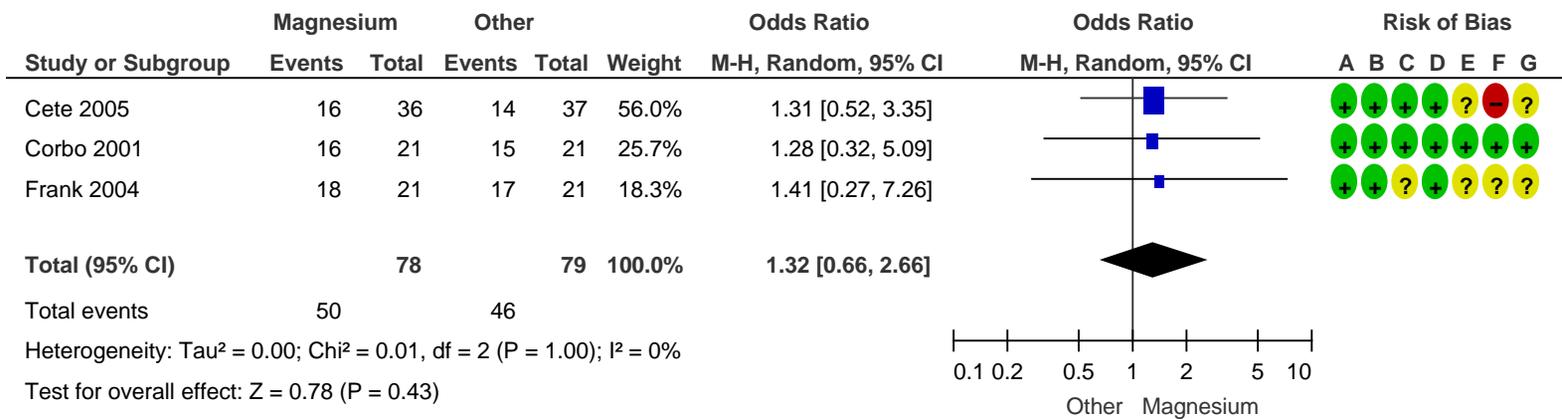
Figure 1. Comparison: Magnesium sulfate (IV) versus Other treatments: Outcome Headache response at 60 min



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure 2. Comparison: Magnesium sulfate (IV) versus Other treatments: Outcome, Adverse effects



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure 3. Comparison: Magnesium sulfate (IV) vs. Other treatments: Outcome: Need for rescue medications